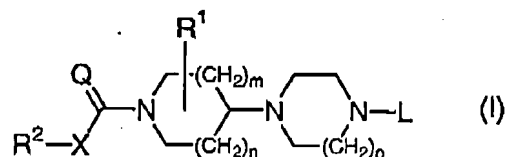


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This listing of claims will replace all prior versions, and listings, of claims in the application:

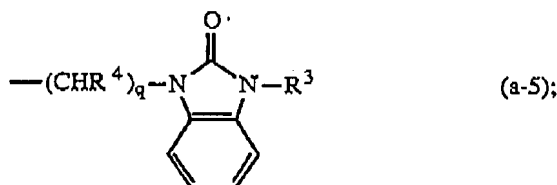
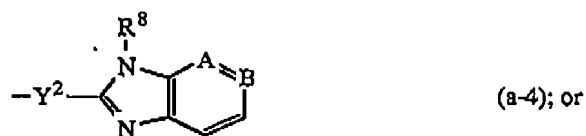
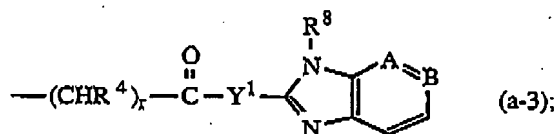
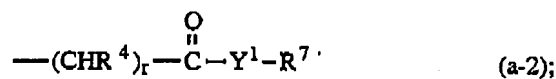
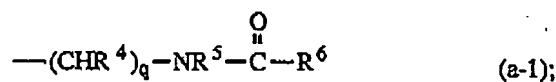
1. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredients, an opioid analgesic and a therapeutically effective amount of a compound according to Formula (I)



the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof, the *N*-oxide form thereof and the prodrugs thereof, wherein

- n is 0, 1 or 2;
m is 1 or 2, provided that if m is 2, then n is 1;
p is 1 or 2;
=Q is =O or =NR³;
X is a covalent bond or a bivalent radical of formula -O-, -S-, -NR³-;
R¹ is Ar¹, Ar¹C₁₋₆alkyl or di(Ar¹)C₁₋₆alkyl, wherein each C₁₋₆alkyl group is optionally substituted with hydroxy, C₁₋₄alkyloxy, oxo or a ketalized oxo substituent of formula -O-CH₂-CH₂-O- or -O-CH₂-CH₂-CH₂-O-;
R² is Ar², Ar²C₁₋₆alkyl, Het¹ or Het¹C₁₋₆alkyl;
R³ is hydrogen or C₁₋₆alkyl;
L is hydrogen; Ar³; C₁₋₆alkyl; C₁₋₆alkyl substituted with 1 or 2 substituents selected from hydroxy, C₁₋₆alkyloxy, Ar³, Ar³C₁₋₆alkyloxy and Het²; C₃₋₆alkenyl; Ar³C₃₋₆alkenyl; di(Ar³)C₃₋₆alkenyl or a radical of formula

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wherein

each q

independently is 2, 3 or 4;

each r

is 0, 1, 2, 3 or 4;

each Y¹independently is a covalent bond, -O- or NR³;Y²is a covalent bond, C₁₋₄alkanediyl or -C₁₋₄alkylNR³;

each -A=B-

independently is a bivalent radical of formula -CH=CH-, -N=CH- or -CH=N-;

each R⁴independently is hydrogen, C₁₋₆alkyl, Ar² or Ar²C₁₋₆alkyl;R⁵is hydrogen, C₁₋₆alkyl or Ar³;R⁶is C₁₋₆alkyl, Ar³, Ar³C₁₋₆alkyl, di(Ar³)C₁₋₆alkyl, Ar³C₃₋₇cycloalkyl, or indolyl;R⁷is Ar³, Ar³C₁₋₆alkyl; di(Ar³)C₁₋₆alkyl; C₁₋₆alkyl; C₃₋₇cycloalkyl; C₃₋₇cycloalkyl substituted with Ar³; oxazolyl; oxazolyl substituted with halo or C₁₋₆alkyl; thiazolyl; thiazolyl substituted with halo or C₁₋₆alkyl; imidazolyl; imidazolyl substituted with Ar³, C₁₋₆alkyl,

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Ar³C₁₋₆alkyl or halo; indolyl; indolyl substituted with C₁₋₄alkyl;
2,3,4-trihydroquinolyl; pyrrolidinyl or furanyl;
each R⁸ independently is hydrogen, C₁₋₆alkyl, C₃₋₇cycloalkyl or a radical of
formula of formula

-Alk-R¹¹ (b-1) or
-Alk-Z-R¹² (b-2);

wherein

Alk is C₁₋₆alkanediyl;Z is a bivalent radical of formula -O-, -S- or -NR³-;

R¹¹ is phenyl; phenyl substituted with 1 or 2 substituents selected from halo,
C₁₋₆alkyl or C₁₋₆alkyloxy; furanyl; furanyl substituted with 1 or 2 substituents
selected from C₁₋₆alkyl or hydroxyC₁₋₆alkyl; thienyl; thienyl substituted with 1
or 2 substituents selected from halo or C₁₋₆alkyl; oxazolyl; oxazolyl substituted
with 1 or 2 C₁₋₆alkyl substituents; thiazolyl; thiazolyl substituted with 1 or 2
C₁₋₆alkyl substituents; pyridinyl or pyridinyl substituted with 1 or 2 C₁₋₆alkyl
substituents;

R¹² is C₁₋₆alkyl or C₁₋₆alkyl substituted with hydroxy, carboxyl or
C₁₋₆alkyloxycarbonyl;

Ar¹ is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected
from the group consisting of halo, C₁₋₄alkyl, haloC₁₋₄alkyl, cyano, aminocarbonyl,
C₁₋₄alkyloxy and haloC₁₋₄alkyloxy;

Ar² is naphthalenyl; phenyl; phenyl substituted with 1, 2 or 3 substituents each
independently selected from the group consisting of hydroxy, halo, cyano, nitro, amino,
mono- or di(C₁₋₄alkyl)amino, C₁₋₄alkyl, haloC₁₋₄alkyl, C₁₋₄alkyloxy,
haloC₁₋₄alkyloxy, carboxyl, C₁₋₄alkyloxycarbonyl, aminocarbonyl and mono- and
di(C₁₋₄alkyl)aminocarbonyl;

Ar³ is phenyl or phenyl substituted with 1, 2 or 3 substituents selected from the group
consisting of halo, hydroxy, amino, nitro, aminocarbonyl, C₁₋₆alkyl, haloC₁₋₆alkyl and
C₁₋₆alkyloxy;

Het¹ is a monocyclic heterocycle selected from pyrrolyl, pyrazolyl, imidazolyl, furanyl,
thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyrazinyl
and pyridazinyl; or a bicyclic heterocycle selected from the group consisting of
quinolyl, quinoxalyl, indolyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl,
benzothiazolyl, benzisothiazolyl, benzofuranyl and benzothienyl; each monocyclic and

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bicyclic heterocycle may optionally be substituted on a carbon atom by 1 or 2 substituents selected from the group consisting of halo, C₁₋₄alkyl or mono-, di- and tri(halo)methyl; and

Het² is a heterocycle selected from the group consisting of 1,4-dihydro-5-oxo-tetrazol-1-yl, imidazo[1,2-a]pyridinyl, oxazolyl and imidazolyl; each of said heterocycles may be substituted with 1 or where possible 2 substituents selected from the group consisting of C₁₋₄alkyl and Ar³.

2. (Previously Presented) A pharmaceutical composition according to claim 1 wherein L is hydrogen; C₁₋₆alkyl; C₁₋₆alkyl substituted with hydroxy; C₃₋₆alkenyl; Ar³; Ar³C₁₋₆alkyl; di(Ar³)C₁₋₆alkyl; Ar³C₃₋₆alkenyl; di(Ar³)C₁₋₆alkenyl; or a radical of formula (a-1), (a-2), (a-4) or (a-5) wherein:
R⁷ is Ar³; Ar³C₁₋₆alkyl; di(Ar³)C₁₋₆alkyl; C₁₋₆alkyl; C₃₋₇cycloalkyl; C₃₋₇cycloalkyl substituted with Ar³; oxazolyl; oxazolyl substituted with halo or C₁₋₆alkyl; thiazolyl; thiazolyl substituted with halo or C₁₋₆alkyl; imidazolyl; imidazolyl substituted with Ar³, C₁₋₆alkyl, Ar³C₁₋₆alkyl or halo; pyrrolidinyl or furanyl;
Ar³ is is phenyl or phenyl substituted with 1, 2 or 3 substituents selected from halo, hydroxy, amino, aminocarbonyl, C₁₋₆alkyl, haloC₁₋₆alkyl or C₁₋₆alkyloxy;
Het¹ is a monocyclic heterocycle selected from the group consisting of pyrrolyl, pyrazolyl, imidazolyl, furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyrazinyl and pyridazinyl; or a bicyclic heterocycle selected from the group consisting of quinolinyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzisothiazolyl, benzofuranyl and benzothieryl; each monocyclic and bicyclic heterocycle may optionally be substituted on a carbon atom by 1 or 2 substituents selected from the group consisting of halo, C₁₋₄alkyl or mono-, di- and tri(halo)methyl.
3. (Previously Presented) A pharmaceutical composition according to claim 1 wherein, R¹ is Ar¹methyl and attached to the 2-position or R¹ is Ar¹ and attached to the 3-position.
4. (Previously Presented) A pharmaceutical composition according to claim 1 wherein, R²-X-C(=Q)- moiety is 3,5-di-(trifluoromethyl) phenylcarbonyl.

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5. (Previously Presented) A pharmaceutical composition according to claim 1 wherein, R^1 is $Ar^1C_{1-6}alkyl$, R^2 is phenyl substituted with 2 substituents selected from the group consisting of methyl and trifluoromethyl, X is a covalent bond and $=Q$ is $=O$.
6. (Previously Presented) A pharmaceutical composition according to claim 1 wherein, n and m are 1 and p is 1 or 2.
7. (Previously Presented) A pharmaceutical composition according to claim 1 wherein, R^1 is phenylmethyl; R^2 is phenyl substituted with 2 substituents selected from the group consisting of methyl and trifluoromethyl; n, m and p are 1; X is a covalent bond; and $=Q$ is $=O$.
8. (Previously Presented) A pharmaceutical composition according to claim 1 wherein, L is a radical of formula (a-2) wherein R^4 is hydrogen or phenyl; r is 0 or 1; Y^1 is a covalent bond, -O- or -NH-; R^7 is pyrrolidinyl; furanyl; 1-phenylcyclohexanyl; diphenylmethyl; or phenyl substituted with 1, 2 or 3 substituents each independently selected from the group consisting of methyl, methoxy and chloro
9. (Previously Presented) A pharmaceutical composition according to claim 1 wherein, the pharmaceutical composition comprises a compound selected from the group consisting of:
 - 4-[1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-N-(2,6-dimethylphenyl)-1-piperazine acetamide;
 - 4-[1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-N-(1-phenylcyclohexyl)-1-piperazine acetamide;
 - 1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-[4-[□-(1-pyrrolidinylcarbonyl)benzyl]-1-piperazinyl]piperidine;
 - 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-[(2-methyl-5-oxazolyl)methyl]-1H-benzimidazol-2-yl]-1-piperazinyl]-2-(phenylmethyl)piperidine;
 - 4-[1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(4-trifluoromethylphenyl)methyl]-4-piperidinyl]-N-(2,6-dimethylphenyl)-1-piperazine acetamide; and
 - 4-[1-[3,5-bis(trifluoromethyl)benzoyl]-2-[(3,4-dichlorophenyl)methyl]-4-piperidinyl]-N-(2,6-dimethylphenyl)-1-piperazine acetamide.

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10. (Previously Presented) A pharmaceutical composition according to claim 1 wherein, the pharmaceutical composition comprises a compound selected from the group consisting of :
- o (+)-(B)-*trans*-4-[1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-*N*-(2,6-dimethylphenyl)-1-piperazine acetamide;
 - o (-)-(B)-*cis*-4-[1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-*N*-(2,6-dimethylphenyl)-1-piperazine acetamide; and
 - o (+)-(B)-*trans*-4-[1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-4-piperidinyl]-*N*-(2,6-dimethylphenyl)-1-piperazine acetamide (L)-malic acid (1:1).
11. (Previously Presented) A pharmaceutical composition according to claim 1 wherein, the pharmaceutical composition is formulated for simultaneous, separate or sequential use.
12. (Previously Presented) A pharmaceutical composition according to claim 1 wherein, the opioid analgesic is one or more compounds selected from the group consisting of alfentanil, buprenorphine, butorphanol, carfentanyl, codeine, diacetylmorphine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, levorphanol, lofentanyl, meperidine, methadone, morphine, nalbuphine, oxycodone, oxymorphone, pentazocine, propoxyphene, remifentanyl and sufentanyl; and derivatives and pharmaceutical acceptable salts thereof.
13. (Previously Presented) A pharmaceutical composition according to claim 12 wherein the opioid analgesic is one or more compounds selected from the group consisting of oxycodone, codeine, morphine, fentanyl, buprenorphine, hydrocodone, hydromorphone and pharmaceutical acceptable salts and derivatives thereof.
14. (Currently Amended) A pharmaceutical composition according to claim 1 ~~where~~wherein, the pharmaceutical composition is in a form suitable to be orally administered.
15. (Previously Presented) The use of a pharmaceutical composition according to claim 1, for the prevention and/or treatment of pain and/or nociception.

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16. (Currently Amended) The use of a pharmaceutical composition according to claim 1, for the prevention and/or treatment of acute and chronic pain, more in particular in inflammatory, post-operative, emergency room (ER), breakthrough, neuropathic and cancer pain treatments.
17. (Previously Presented) The use of a pharmaceutical composition according to claim 1, for the prevention and/or treatment of emesis in opioid-based treatments of pain.
18. (Previously Presented) The use of a pharmaceutical composition according to claim 17 for the prevention and/or treatment of nausea and vomiting in opioid-based treatments of pain.
19. (Previously Presented) The use of an NK₁-receptor antagonist, in particular an NK₁-receptor antagonist according to Formula (I), the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof, the *N*-oxide form thereof and prodrugs thereof, for the prevention and/or treatment of respiratory depression in opioid-based treatments of pain.
20. (Previously Presented) The use of an NK₁-receptor antagonist, in particular an NK₁-receptor antagonist according to Formula (I), the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof, the *N*-oxide form thereof and prodrugs thereof, for reducing and/or overcoming the tolerance observed with opioids in opioid-based treatments of pain.